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THE MIDDLETON-GOLDSMITH LECTURE
FOR 1890,

Delivered before the New York Pathological Society, Jan. 15, 1890.

BY

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OF PHILADELPHIA.



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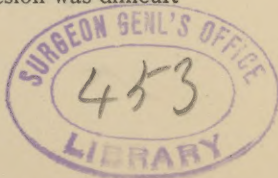
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MR. PRESIDENT AND MEMBERS OF THE NEW YORK PATHOLOGICAL SOCIETY: Your President's kind introduction adds to the embarrassment which I confess to have felt in endeavoring to select some subject which might more or less worthily occupy the attention of such a body; in casting about for such a subject, I found much difficulty, and that which I finally chose will possibly be regarded as scarcely appropriate. It is not wholly pathological, but partly clinical in its interest. The very name "hepatic fever" may seem more or less a misnomer. We meet with so many affections of the liver attended with fever, that it would be impossible to place in one group all to which this name might in one sense be applied.

It is true that, without calling in the assistance of our willing brethren, the laparotomists, we are, at times, unable to make an exact differential diagnosis, and are still forced to name the affection by the most prominent symptom. And I am sure you have all met with cases of lesion of the liver or of its ducts, attended with fever of the peculiar type I wish to describe, and in which the determination of the exact seat and kind of the lesion was difficult



or impossible. I do not intend to speak of the more ordinary fever which attends many acute hepatic affections, which is merely a more or less severe continued febrile movement with moderate fluctuations. We note this, for instance, in acute catarrhal jaundice, or for a few days following the passage of a gall-stone. Nor do I now include that very interesting affection, known as Weil's disease, of which, I believe, I have seen three cases, although only in one have I a full clinical and pathological record. What I shall say is based on a study of twenty-one cases, where fever of a peculiar paroxysmal character appeared in connection with various hepatic lesions. It may either be a quotidian, a tertian, or a quartan; and I have even seen a double quotidian type. It is a distinctly paroxysmal fever, often ushered in by a violent chill, shaking the whole body of the patient. Sometimes there is only a slight rigor, sometimes it even comes on without any perceptible sensation of cold at all. This is followed by an unusually rapid rise of temperature, reaching as high a point even as 103° , 104° , or 105° , attended with distress, restlessness, thirst, more or less pain through the frame, and not rarely with vomiting; lasting for a few hours—from four or five to as many as ten or twelve—and terminating by a sweat, sometimes merely a moisture, sometimes a drenching sweat soaking the clothing of the patient and bed. This fever may be repeated, as I have said, at quotidian, tertian, or quartan intervals; a single paroxysm may close it, or there may be successive paroxysms, the intervals being sometimes regular and sometimes wholly irregular, amounting to days, weeks, or even months before another attack appears. After each paroxysm, jaundice makes its appearance as a rule; but sometimes it is only slight, or may even be absent, with at most a little yellowish discoloration of the conjunctiva and some darkening of the urine for a short time. In the majority

of cases, however, the jaundice is decided, and may be intense, lasting for varying periods, sometimes days, sometimes several weeks, before passing away. At the moment of the occurrence of such a paroxysmal fever, there may or may not be severe hepatic pain. This pain may be wholly absent, and yet a hard chill, high fever, profuse sweat, and deep jaundice follow. Or there may be pain so severe that it forces the belief that a calculus is engaged in one of the ducts—the pain requiring hypodermic injections of morphine for its relief.

In bad cases, where such paroxysms recur, you can easily understand that the general health of the patient suffers severely. Anæmia is developed; there is marked loss of flesh; the digestive processes are impaired; and we find these paroxysms recurring with greater and greater facility; in fact, in this type of hepatic fever, an unfavorable prognosis often has to be made, and many such cases go on to a fatal result after a course of variable duration. But it is far from being always fatal, and in a certain number of cases—it has been my own good fortune to see quite a number of them—after having from fifty to one hundred paroxysms, complete recovery occurs, without anything to signalize the termination of the process—no morbid discharge, nor passage of a calculus, but a gradual subsidence of the morbid condition itself.

It is to this type of fever, paroxysmal and intermittent as a rule, with paroxysms occurring sometimes closely together, with a certain amount of febrile action kept up between them, that I would ask your attention this evening.

It is not in connection with the liver alone that we meet with fever of this type; I shall later ask attention to the resemblance existing between this and urethral fever, where we find in connection with certain morbid

states of the urinary tract, febrile paroxysms having considerable analogy with those already described.

In trying to understand a febrile process of this kind, it is clear that we must have in view the general causation of fever, and I take it, that we are all agreed to-day that fever comes very often as a septic process from absorption into the system of some morbid, pyrogenic, poisonous substance. And, secondly, that fever is caused by a disorder of the nervous apparatus controlling heat production and dissipation, and that this disorder may either be centric directly, or may be induced by reflex irritation from some local disease. The reality of this last cause of fever, I think, may be demonstrated by the interesting physiological experiments which my distinguished friend, Dr. H. A. Hare, is bringing to a conclusion in the laboratory of the University of Pennsylvania, which show that a lesion which engenders fever will not do so provided all the nerve-trunks of the limb be severed; in other words, that in certain cases we must recognize, as a cause, the existence of a local lesion acting upon the heat-controlling mechanism at the centre in a reflex manner.

When we come to apply these general thoughts upon fever to the subject of fever connected with the liver, we would expect, I think, from the known antiseptic properties of the bile, to find certain difficulties in the development of fever; whereas, on the contrary, it seems to me, clinically, that there is no organ in connection with which we find more violent explosions of fever than we do in the case of the liver. It is very certain, however, that the entrance of bile into the blood cannot be brought into account to explain the production of fever. The injection of the entire bile, or the injection of bile-salts, both lower temperature, slow the pulse, and slow breathing, but do not create fever at all. Again, bile may lie for a long time, even for weeks, in an obstructed

duct, and undergo no morbid change which makes it pyrogenic. It is perfectly true that the bile, a highly complex liquid, is singularly prone to undergo chemical change—bilirubin becomes converted into biliverdin in the easiest manner possible. But this is a chemical change, and is not one attended with the development of septic principles; so that the bile may remain a long time in the obstructed dilated ducts without undergoing changes rendering it capable of producing septic processes or pyrexia.

It seems, then, necessary, in these cases, that we should recognize the existence of additional elements; that there should be mixture with the bile of morbid discharges from the mucous membrane of the ducts; and it is very clear that this could be brought about in almost any case very readily. Thus, for instance, the passage of a gall-stone frequently leaves a laceration of the mucous membrane. We have, then, at once an abrasion, a source of morbid discharge and admixture with the bile of putrefactive matter, and this may be sufficiently considerable in amount to alter the character of the bile and start a septic process.

Or, again, this same lesion serves as the starting-point of reflex irritation, to disorder the heat-controlling mechanism. Note, in connection with this, that most of the cases we are discussing are attended with more or less obstruction of the ducts of the liver, and think how often it is, in studying our cases of liver disease, that we recognize the existence of such obstruction. Now, when the ducts of the liver are obstructed and distended with accumulated bile, not only is the bile absorbed into the lymphatics if the pressure goes beyond a certain point, causing absorption-jaundice, but this pressure upon the hepatic tissue about the distended ducts interferes powerfully with the functional activity of the liver.

The bile-secreting function of the liver is certainly far

from being its only important function. I doubt not we have yet to learn of new functions of essential value; but there is one we already know enough about to assert that it is of immense importance, and, so far as the production of disease is concerned, of even greater importance than the bile-secreting function, *i. e.*, the ptomaine-destroying function of the liver.

The liver, then, possesses this extraordinary power of arresting pyrogenic substances such as the albumoses, whether hemi- or deutero-albumose, as they are passing into the system from the intestinal canal, and of destroying their morbid properties. So that, granting the functional activity of the liver, these pyrogenic substances are not able to penetrate the system and generate pyrexia.

If you have a condition of the liver where the bile-ducts are distended with accumulated bile, not only, I say, does jaundice occur, but inevitably we shall have this important ptomaine-destroying function of the liver more or less paralyzed; and there will pass on into the system, on account of this arrest of the functional activity of the liver, pyrogenic and poisonous substances which may be responsible for the fever and other symptoms which subsequently develop.

The mere absence of bile from the intestine in cases of occlusion, even though it be a complete absence, is not immediately disastrous provided the diet of the patient is carefully regulated, and especially if fats be excluded; for, in the absence of bile, the fats break up rapidly into highly injurious derivatives in the intestines.

Thus I may quote the case (No. 1) of William McF., a man aged sixty-five years, who was admitted to the medical ward of the Philadelphia Hospital on September 2, 1870. The history obtained showed that he had enjoyed good health until four months before admission, when jaundice gradually appeared. The yellowness grew steadily more and more marked, and he lost flesh and strength rapidly.

He had never suffered from an attack of hepatic colic, and the present sickness had come on without pain. On admission the jaundice was intense, affecting the conjunctiva and the whole cutaneous surface. His mind was clear but dull, and he usually lay in an apathetic, lethargic state. His weakness was so great that he rarely left his bed, and his emaciation was extreme. There was entire anorexia; the bowels were constipated, and the stools grayish-white in color, tough, and very offensive. No free fat was observed in the stools. The urine was rather scanty, and contained no albumin, but was dark brown in color. Tests showed the presence of abundant bile-pigment, but on applying to it Hoppe's test for bile-acids, none were detected. The abdomen was meteoric. The area of hepatic dulness was normal, and no tumor or irregularity of the surface of the liver could be felt. The gall-bladder could not be detected. There was no tenderness over the liver. The skin was usually dry; perspiration, when it occurred, was deep yellow. There was at no time any fever.

At the autopsy all the viscera were deeply stained yellow. The kidneys contained numerous large cysts. The liver, of normal shape, was somewhat enlarged in size, but much more dense and heavy than normal, weighing five pounds. The liver tissue was deeply stained with bile, and coarse-grained, as though in the first stage of cirrhosis. The radicles of the gall-ducts throughout the organ were much dilated and filled with grumous bile. The larger branches of the hepatic ducts, as the transverse fissure was approached, contained numerous polygonal brownish-black gall-stones. The hepatic duct itself was enormously dilated (at least one inch in diameter), and was filled with very numerous calculi. These calculi, for the most part, measured one-fourth to one-third of an inch in diameter. There was one, however, fully two-thirds to three-fourths of an inch in its meas-

urements, and with rounded edges, which was firmly impacted in the hepatic duct, just above its juncture with the cystic duct. The common duct itself was somewhat dilated, either from the previous passage of smaller calculi, or, more probably, from the dilating action of the impacted stone. The gall-bladder was considerably distended with light-colored bile, and contained numerous minute blackish calculi. There was no thickening, inflammation, or ulceration at any point of the biliary passages.

Here had been prolonged and entire occlusion of the hepatic duct, and yet no hepatic fever had resulted, because at no point in the biliary passages was there evidence of abrasion or inflammatory action; there had simply been resorption into the body of the normal bile. The patient's health had suffered from this protracted occlusion very much more markedly than was observed; for instance, in the well-known case reported by Bristowe, of London, where, for a long time, a patient was under observation with a biliary fistula. A tube had been introduced into the duct so that all the bile escaped externally, none entering the intestine, as shown by the condition of the fæces and of the local lesion, and yet there was very fair maintenance of the patient's health. There are a few similar cases on record. I will add the record of another interesting case of obstruction of the bile-ducts without fever, which was under my care lately.

CASE II.—H. N. B., aged seventy-five, began to feel sick December 20, 1887, at which time he weighed one hundred and sixty-five pounds. Twelve years previously, about 1876, he had a spell of pain followed by jaundice. He also had several spells about 1883. Subsequently he was pretty well up to September, 1887, after which he had occasional slight attacks of pain in the region of the liver, followed by a little jaundice, and then had a severe attack on December 20, 1887,

and a second one in February, 1888. After this they occurred almost every week and the jaundice was constant, though fluctuating in degree and passing away somewhat in the intervals. He had no fever at any period in the course of his case, but had, however, occasional sweats, chiefly of the legs.

He came under my care in April, 1888, when he was losing flesh rapidly and was constantly deeply jaundiced. The urine contained bile, but the fæces were not putty colored. Examination showed slight enlargement of the liver, but no mass could be found nor was the gall-bladder distended. There was no tenderness on pressure over the liver, but only a deep-seated sense of discomfort. He continued to have occasional spells of pain, with deepening jaundice but without fever, until summer, when he went to his country seat and I saw him but occasionally. He now had a series of very alarming spells with slight chills, followed by pain, prostration, and sweating, but without fever; there was constant deep jaundice. On July 8th, he had an alarming spell, during which he fainted and immediately afterward discharged a large amount of golden-yellow thick bile by the bowel, estimated at two pints. He continued to discharge this in smaller amounts for three days and then seemed to improve. On July 28th he had his worst spell, fainting and lying unconscious for an hour and a half. After this attack the pain, which had always been over the liver, about the short ribs on the right side, suddenly changed and was in the middle, below the umbilicus; and he never had any pain in the hepatic region afterward. From this date until October 31st, every stool was examined but no calculus was found. The stools were very varied, sometimes in ribbon shape, sometimes round; but whether flat or round, they were always grooved as if forced past some round hard object. Their color was at times

brown, green, and white, and at other times there was a light green liquid, but no pus was seen. From July to December he had numerous spells of pain always low down in the middle of the belly; and in such attacks he always had impaction of the cæcum, requiring laxatives, which would bring away ribbon-shaped fæces. After August his only treatment was rest, massage, careful diet, and olive oil. He was so reduced that he weighed only one hundred and ten pounds, and so very anæmic that he fainted on several occasions. His last spell of pain was on November 25th, after which he gradually and steadily improved. He is now in perfect health, in his seventy-eighth year, and weighs as much and can walk as briskly as at any time for years past.

I believe that this case was one of large calculus with accumulation of bile behind it; and that the calculus escaped into the intestine and remains fixed there, probably in a pouch of the colon, up to the present time.

I have spoken thus of the mere occlusion of the bile-ducts, and of the fact that they often give rise only to these distention-results without hepatic fever. It is probably true, as already stated, that extreme distention may favor the admission of pyrogenic substances by impairing the ptomaine-destroying function. But it must also be noted that after occlusion has lasted some time, the irritation of the wall extends to the connective tissue surrounding the duct, and we have set on foot a peri-angiocholitis, which may spread, more or less extensively, through the organ. Not only this, but when morbid discharges occur and mix with the retained bile, we may find either a large abscess or a number of small miliary abscesses scattered through the liver even to the capsule. Thus it is that in some cases of occlusion we have no fever, and in others the typical form described is present.

If we now try to explain the apparent periodicity which occurs in some cases of hepatic fever, it seems

attended with considerable difficulty. If there be a fixed lesion, as, for instance, a suppurative inflammation of the gall-bladder, there we have a distinct pus-forming centre, and we may have a true pyæmia. Naturally, in such cases, we find an explanation for the febrile process with regularly recurring, often quotidian paroxysms, just as we find with a pus centre of similar character elsewhere in the body. But in those cases, and they constitute the majority of the cases, where the paroxysms do not recur every day or every third day, or with any regularity, and yet recur frequently, it seems as if we must assume the existence of a lesion not continually sufficient to cause fever, but which is extremely liable to be increased by external causes.

Take, for instance, a catarrhal angiocholitis, an inflammation of the bile-ducts of a catarrhal character, with a certain amount of thickening of the walls of the ducts, and a relaxed and enfeebled condition of the system; here is a state singularly prone to exacerbation and increase from external causes—such as a chilling of the surface or an indiscretion in diet; increased swelling of the mucous membrane and total occlusion of the ducts are the results, and there is a mixture with the bile of the morbid discharges from the inflamed mucous membrane, and at the same time an intense local irritation acting upon a system which has become highly sensitive.

I shall read to you the notes of a case where a long-continued series of these paroxysms were evidently explicable on this supposition.

CASE III.—H. B. D. came under my care on March 19, 1888. For many years he had been greatly exposed on the plains in the West, subsisting on coarse food. His best weight was one hundred and fifty, but for twenty years it was not above one hundred and thirty-five. In 1880 he had congestion of the lungs in Texas,

and has been susceptible to colds since then, catching cold frequently every winter. He had diarrhœa through the summer of 1885; and again in the summer of 1887. He was in the West, exposed to intense heat, and had returned to Nantucket, where in August he had his first chill, and has had chills since then at irregular intervals, from daily up to seventeen days apart. The chills were severe at times, lasting distinctly for an hour. They were followed by fever ($102\frac{1}{2}^{\circ}$ to 104°), ascending for from six to twelve hours and then quickly dropping, so that the temperature within two or three days was almost normal. No treatment prevented their return. At about the same time (September, 1887), pain began to be felt in the right side; but on one occasion only were the chill and attendant pain so violent that hypodermic injections of morphine were required. Jaundice first appeared in October, 1887, and has continued more or less since, at times very deep, at other times almost absent. It always comes promptly after a chill, when the urine also becomes very high-colored. The stools are light but never clay-colored, and always have contained bile.

When I first saw him I made the following note: the chills now recur about twice a week, but irregularly. The patient has progressively lost flesh and strength. Ascites appeared February 15, 1888, and has increased, so that now it is very considerable. The urine contains a small amount of albumin, specific gravity 1021 to 1023; with abundant indican at all times. It was extremely difficult to obtain the reaction of biliary coloring matter, and repeated tests gave negative results. But on getting the urine perfectly fresh and preventing decomposition of the bilirubin by the addition of a little ether it was obtained. This observation seems important as bearing on the rapidity with which the organic bodies in the bile may break up, whether or not from bacterial

action, and thus bearing also upon the development of irritating ptomaines in obstructed bile-ducts.

The diagnosis adopted was that of severe catarrhal angiocholitis, and the result verified it. Paracentesis of the abdomen was performed three times and several gallons of clear yellow serum were withdrawn each time. The patient was treated with absolute rest in bed, rigidly strict diet, and alternating courses of nitrate of silver and potassium iodide. He took at first twenty-five grains of silver, then after an interval of a month fifteen grains, after another interval fifteen grains more, and subsequently took it at short periods when spells recurred. Careful study showed that there had been no periodicity in the chills and that they had always been produced by exertion and exposure. He had finally become so sensitive that the most trivial exposure was sure to be followed by a severe chill. The ensuing fever, running up to 103° or 104° , was followed by profuse sweat, intense jaundice, and furious itching. His restless spirit led him to rise as soon as he was able, and immediately after doing so there would come another spell. In this way a certain semblance of regular recurrence was produced. After he was confined to bed the spells subsided and soon ceased; and he had none as long as I kept him in bed, which was nearly four months; at the end of which period he was almost free from jaundice, had no ascites, and had gained flesh and strength. He immediately began to overtax his strength and to expose himself. He would then take cold and have a recurrence of jaundice; but as the tone of his system improved, and with the improvement in the local conditions, there was continually less and less fever with the spells, though it was not unusual for it to go up to $101\frac{1}{2}^{\circ}$ and 102° . The urine continued to contain a trace of albumin, and occasionally a hyaline cast would be found. The blood showed, at different times, from

sixty increasing to eighty-five per cent. of hæmoglobin and from 3,400,000 up to almost normal of red-blood globules. His improvement was thus progressive but fluctuating and the case required constant, close watching. For instance, after being entirely free from fever and jaundice, all summer at Nantucket, he overtaxed and exposed himself in September, 1889, in New York, and brought on a chill with high fever and return of jaundice, which confined him to bed for more than two weeks. Since then he has improved steadily and is now in very good health. He is travelling in the West and is using a drachm of glycerin twice daily with potassium iodide.

In the following interesting case the symptoms and the course of the disease were very similar to those just narrated.

CASE IV.—Henry E. K., aged forty-nine, seen in consultation with Dr. E. E. Montgomery. He had catarrhal fever with jaundice, in August, 1889, and since then has not been well. He is a finely built, large man, who had not had a day's illness in thirty years. He is abstemious in habits, but has worked very hard and had much responsibility. During the past two or three years he has had several mild attacks of hepatic colic, but no jaundice. He was slightly jaundiced in September, and then had chills and fever of tertian type for several weeks, which were not controlled by quinine. The chills varied in intensity, being sometimes slight, but occasionally severe, with shaking. They occurred at different periods of the day, but usually in the morning, and were followed by fever, of from 102° to 104° , lasting into the night, and ending with a sweat during the night, so that the temperature was down on the following morning. The jaundice that followed was variable both in depth and duration. During twenty-four hours, when he had one of these spells, he passed about thirty-five

ounces of urine containing 1.9 per cent. of urea, or about 300 grains in all. The appetite was poor, the stools clay colored and either loose or costive, but he had no severe pain or soreness in the region of the liver. On November 1st he had a sharp chill, and three days later a mild chill, and then violent pain and deep persistent jaundice. He continued to have chills and fever with increasing frequency throughout November and December; they would recur upon any exertion or exposure. Even after he was kept continuously in bed and upon an exclusive milk diet, he had several, but with decreasing severity and at increasingly long intervals. There were fulness and a slight sense of resistance in the region of the gall-bladder, with slight relative impairment of resonance over the duodenal region. No calculus was ever found in the fæces. He was confined rigidly to bed for a number of weeks. Repeated blisters were applied over the region of the gall-bladder. He took alternating courses of silver nitrate with opium and belladonna and of potassium iodide. The jaundice has now completely passed away. There has been no spell for a considerable period; he is rapidly regaining flesh and strength.

Without dwelling upon a question of diagnostic interest, I would call special attention to the importance of estimating the daily amount of urea excreted during such paroxysms, in order to establish or refute Regnard's statement that, in distinction with what occurs in malarial paroxysms, the amount of urea excreted is reduced in hepatic fever.

In considering the mechanism of attacks in such cases as these, we are struck by the presence of intense local irritation and of probable septic action. There is occlusion of larger or smaller branches of the bile-ducts— not necessarily of the main duct, since bile may be constantly present in the fæces— so that the network of ducts in only a small area of the liver may

be involved and the mucous membrane be in a state of chronic catarrhal thickening. After each of the first few paroxysms the patient promptly returns to his usual habits and, sooner or later, induces a renewal of inflammation with obstruction and all the symptoms of an attack. The system soon passes into a morbidly sensitive and pyrogenic state; the heat-controlling mechanism becomes so easily disturbed that mere reflex irritation from a spot of exaggerated catarrhal inflammation may suffice to bring on a spell: but, in addition to this, the lesion of the mucous lining of the affected bile-ducts becomes more and more serious, and complete obstruction more and more readily produced. The morbid discharges from the inflamed mucous surface, which have been escaping with the bile, are then retained and induce septic changes in the contents of the ducts. There is thus the double element of acute local irritation acting on a system in a state of exaggerated sensibility, and a source of septic infection acting on a system where the ptomaine-destroying function of the liver is more or less impaired from the distention of the ducts.

It will be seen at once that in such cases the diagnosis from hepatic abscess must be considered with the greatest care. Certainly in Case III. (H. B. D.) it seemed at first as though there must be grave organic disease. A careful consultation was held in regard to laparotomy after the first paracentesis; but after repeated examination I was unable to satisfy myself that the condition justified even exploratory puncture. After prolonged confinement to bed, it became evident that the hepatic fever was not connected with a fixed suppurating centre from which septic absorption was taking place, but was connected with a varying degree of angiocholitis, and that the gravity of the symptoms was even more dependent upon the constitutional condition of the patient than upon the seriousness of the local lesion. The com-

plete recovery of the patient has confirmed this view, and the rapid progress of H. E. K. toward recovery justifies a similar diagnosis in his case.

While it is true that, in occlusion of the ducts, there may be only dilatation of the smaller ducts above that point, with alteration and atrophy of the cylindrical epithelium and, of course, with some interference with the functional activity of the liver; it must not be forgotten that there is constant danger of such dilated ducts becoming attacked with inflammation which will rapidly result in more serious lesions. The retained bile becomes grumous and decomposed, containing shreds of detached epithelium and flakes of muco-pus; suppuration occurs in the connective tissue adjacent to the ducts, and a section of the liver may show disseminated miliary abscesses, sometimes closely clustered around the main duct and sometimes situated at the ends of minute ducts, so as to show as yellowish points immediately under the peritoneum. In other cases the process may go on to the production of a large single hepatic abscess. In cases where such suppuration is escaped, but where the angiocholitis is severe and deeply seated, the inflammation of the connective tissue around the ducts may go on to the gradual production of one type of cirrhosis of the liver; and you are all doubtless familiar with this development as a result of recurring catarrhal inflammation of the bile-ducts.

While, however, the cases above reported show that even when there have been very grave lesions, doubtless short of actual suppuration, the insistence upon protracted rest and rigid hygiene with suitable treatment may cause a gradual subsidence of the angiocholitis with return of the functional activity of the liver, I suspect that in the great majority of cases of hepatic fever, such as I am describing, there is pus present at some point about the liver. The suppuration may, as in the following

case, be seated in the gall-bladder and also take the form of a miliary abscess close to the peritoneum ; of course, defying operative interference.

CASE V.—Mr. F., aged sixty-three, consulted me on September 16, 1889. He had typhoid fever in 1882, and since then had often had pain in the back of the head. In the spring of 1887 he had several spells of hepatic colic—in all probability with gall-stone—followed by deep jaundice and intense itching. In the intervals between these spells he apparently regained his usual health, but for the past year had clearly been failing. He had lost much flesh, had suffered from insomnia, and recently albumin had been detected in the urine. He had also had several severe spells of hepatic pain, each time followed by fever and by local tenderness and deep jaundice. Thus, in March, 1889, he had a severe spell of pain in the region of the liver, lasting nearly all day, followed by jaundice for six weeks with severe itching ; and another in April ; but all was cleared up in June or July. He had another spell in August, and had been deeply jaundiced since then, and his general condition had failed more rapidly. I found his urine, with a specific gravity of 1010 to 1013, neutral or slightly acid, with a moderately thick ring of albumin, and with quite numerous epithelial and granular casts ; no sugar. This condition of urine persisted until his death, on November 12th. There was marked tenderness over the bile-ducts. In spite of continued rest in bed, and with very careful diet, repeated small blisters, and, internally, silver nitrate with belladonna, and olive oil, he continued to have, at short intervals, recurring spells of pain, followed by deeper jaundice, worse itching, and more tenderness. In each of these spells there was distinct fever, but he had no severe chill until about November 1st. From then until death he had, almost daily, a violent chill with chattering of teeth, followed by

rise of temperature to 105° and ending in a profuse sweat. The jaundice now subsided decidedly, although he still remained somewhat yellow. The stools had never been putty colored, but only yellowish, and now were brownish. The urine cleared up, but continued to show the features as before stated.

Post-mortem held thirty hours after death. Body somewhat emaciated; jaundice marked; rigor mortis present.

Abdomen alone examined. On section, there was found a good layer of fat in the subcutaneous tissue of the abdominal walls. All of the tissues bile-stained. Omentum very lightly adherent by fine bands to the parietes at scattered points. The liver protruded below the costal margin about three-fourths to an inch; was adherent over the posterior, upper, and right lateral surfaces to surrounding parietes of abdomen, by universal adhesion rather than by bands. This adhesion was most marked posteriorly, where considerable difficulty was experienced in liberating the organ. There was no collection of pus in the peritoneal or retro-peritoneal spaces. *Spleen*: Large, soft, and of a pinkish-buff color. Pulp diffuent and grayish, but without purulent character; typical high temperature spleen. *Kidneys*: Large and coarsely lobulated. Capsule stripped off with moderate ease. On surface of right kidney was a cyst of about the size of a marrowfat pea, containing dark fluid. Surface of organs finely granular. On section: vessels distinct and striation very plain; slight decrease of cortical area. Pelvis and ureters normal.

Stomach, duodenum, pancreas, and liver were removed together. The *pancreas* was partly bisected and a probe placed in the duct, which was found to enter the duodenum at the papilla in the normal position. The gland tissue was, to the naked eye, normal. The *duodenum* and *stomach* were opened along their anterior face, and

were found to be normal. The pyloric ring was of proper calibre.

The *liver* was large, rigid, and firm, of a slate color, and with rounded edges, which gave a feeling of tenseness when pinched. Round ligament normal. The gall-bladder was only found after prolonged search and careful dissection through the surrounding thickened, dense connective tissue. On pressure, the gall-bladder was found to contain fluid, but could not be emptied by pressure. No stone could be felt through the walls. On opening, it was found to contain about half a drachm of thick, creamy pus. On careful probing, a fine orifice was found, which traversed a band of adhesion uniting the tip of the bladder to the duodenum and of a length of about one-half inch, the probe entering the duodenum about one inch below the pyloric ring. The hepatic artery was normal in size and position, as was also the portal vein. The common bile-duct was at first mistaken for the portal vein, by reason of its size. On slitting up the common bile-duct its wall was found to be thickened, its cavity dilated to finger size or larger, and its mucous membrane thickened, rugous, and in places mammillated. The cystic duct appeared as a cul-de-sac branching from the common duct and resembling it in calibre, character of mucous membrane, and thickness of wall. No communication with the gall-bladder existed. There was no ulceration of the mucous membrane, which was studded with the enlarged orifices of glands. On following up the dilated common into the dilated hepatic duct the same increase of calibre was found. This distention was traced up throughout the branches in the liver, even in some places to the periphery of the organ, where they resembled the ends of glove-fingers. On slitting up one of the ducts in the liver it was found to open into a marble-sized pus cavity close to the surface of the liver, the pus contained being thick and pink-

ish. The liver section was granular, coarse, friable, and nutmeg in appearance; evidently fatty and cirrhotic.

Again, in the following case, No. VI., very similar, though even more aggravated, lesions were found.

CASE VI.—I saw Dr. C. G. E., in consultation, in Binghamton, N. Y., on July 5, 1880. He was thirty years of age, and had enjoyed good health. His father and his younger brother had suffered from hepatic colic. He himself had been liable to such attacks for seven or eight years, but, after a trip to Europe five years ago, they seemed to have been arrested; but again, in the past three years, he had six or seven attacks. These apparently were attacks of catarrhal inflammation, with spasm of the bile-duct, but followed by very little organic change. On no occasion did they compel him to abandon his work. During the spring of 1880 he had been unusually busy, and had lost a good deal of rest. He was taken ill about the 14th of June with a chill, pain in the back, subsequent fever, and an intense pain in the region of the epigastrium and gall-bladder. Repeated hypodermic injections of morphine were needed to control the pain. There were several quite severe chills in the first thirty-six hours, with copious vomiting of bilious matter, while the temperature ran up after each chill to $105\frac{1}{2}^{\circ}$. He took calomel freely, in addition to the morphine; and later, when the tendency to return of chills showed itself, quinine was given in full doses. He continued to complain constantly of great pain about the gall-bladder. Vomiting ceased, but there was a tendency to hiccough. The temperature subsequently ranged from 102° to 103° . The tongue was heavily coated and dryish. There was a slight tinge of sallowness, but nothing amounting to marked jaundice. Examination showed an area of dullness in the region of the gall-bladder, extending three inches below the ribs. It was evidently not the distended

gall-bladder, but appeared to be a partial enlargement of the right lobe of the liver, with matting of the adjacent tissues. It appeared indurated, and, on pressure, was very tender but without fluctuation. The fever was markedly hectic in type, with tendency to profuse sweats at night. The urine was discolored and contained bile. The stools were brownish and even at times blackish, though probably from bismuth. The urine contained no albumin. The general liver dulness did not extend above the normal limit, nor did it extend uniformly below the margin of the ribs; but there was a very distinct semi-circular area of greatly impaired resonance and increased resistance, with exquisite tenderness on pressure, which extended from the right nipple line to the median line, and from the lower margin of the ribs downward about two inches.

He did well from July 5th to July 11th, when there was a violent chill, followed by very high fever and cold sweat, leaving him much exhausted. There was still no decided jaundice. After this, he continued to have irregular chills with high fever.

I visited him again on July 24th. He was then extremely weak, with a glazed, dry tongue and thready, frequent pulse. The abdomen was distended. The area of dulness previously described was even more marked. There were decided hectic symptoms, though no distinct chill had occurred since July 12th. As the signs of internal suppuration were so clear, I proposed an exploratory puncture, which was agreed to. I introduced a medium sized trocar about half an inch below the margin of the ribs, in the region of the gall-bladder, and in a direction upward and backward to a depth of two and a half inches. However, nothing but a few drops of blood entered the vacuum. He died within a few days afterward, and the post-mortem examination

showed that there was no gall-stone and no obstruction of the main bile duct. The gall-bladder was the seat of chronic inflammation; its walls were thickened and its cavity greatly contracted. It contained muco-purulent matter. There was marked circumscribed plastic peritonitis around it. The central portion of the liver was much enlarged, and extending upward into this area for a distance of several inches, and occupying a space of four inches in width, there were clustered around the lines of the bile-ducts numerous small abscesses. These varied in size from a pea to a hazel-nut. In some instances the abscess cavity connected directly with the bile-duct, and it seemed as though it might be a collection of pus in a dilated duct. More probably, however, the limiting wall was of morbid formation. The bile-ducts throughout the liver were distended, and there were a few small abscesses at distant points of the organ, near the capsule.

Without entering into the highly interesting questions of diagnosis connected with these cases, I may point out that, in the latter case, the manifest enlargement of the liver in the region of the gall-bladder called for exploratory puncture, although the symptoms had led me to expect disseminated miliary abscess, as indeed was found to exist. Did time permit, I would be glad to describe to you cases of uncomplicated purulent inflammation of the gall-bladder with similar fever, and also the more familiar type of case where a large calculus escapes from the gall-bladder by progressive ulceration, opening into the intestine. I have seen a number of cases of this kind attended with typical hepatic fever of great severity, lasting for many weeks, and yet terminating in recovery. In one such case, which I have published elsewhere, the patient died, years after, of pneumonia and the autopsy showed complete

obliteration of the gall-bladder and cystic duct, so that the middle finger could be passed directly from the duodenum into the dilated ducts of the liver. The gall-stone was found in one of the pouches of the colon. In the following case, on the other hand, there is every reason to believe that the recurring attacks of angiocholitis resulted in the formation of a single large hepatic abscess. It is notable that, in connection with the violent outbreaks of fever, there was neither intense pain nor deep jaundice. It can scarcely be doubted, however, that the origin of the pus evacuated by stool was from the liver.

CASE VII.—A. B., aged forty-six, married, has been exposed to very bad air in the court room, and had also drank water freely from a dirty receptacle. Last spring and through the summer, had intestinal indigestion, with tendency to looseness of the bowels. This fall he assumed additional labor as professor in a law school. After great exhaustion and loss of sleep, was taken with fever; heavily coated tongue, foul breath; temperature 103° to 104° ; urine heavily loaded, and contained some bile. No characteristic spots, no nose-bleeding or bronchial symptoms. The case ran a course for three weeks like an irregular typhoid. He was apparently improving, and his temperature was down when he had a chill while in bed and while still on liquid diet, so that there was no apparent cause. The temperature went up to $104\frac{1}{2}^{\circ}$. The following day it fell almost to normal, but rose again in the afternoon, and so on three successive days. At this time there was discomfort in the hepatic region. The urine contained more bile, and there was slight jaundice. He again improved, and the fever almost disappeared, but in two weeks there was a similar recurrence of chills with high temperature. He had taken abundant quinine from the beginning of the case until this time. There

was a repetition of the same hepatic symptoms. After this there was again improvement, even more marked than formerly. At this time there was a mild attack of phlebitis of the right leg. After this he again improved, and for more than three weeks was free from fever; he began to sit up for several hours daily, and cautiously resumed solid food, when, on December 20th, after taking a greater variety of solid food than he had done before, he was again attacked with chills, the temperature going up to 104° and over, and recurring on three successive days, with similar hepatic symptoms. At no time had the tongue become clean or the breath sweet, though it was much improved before this last attack.

He had taken, with apparent advantage, cool water enemata of about one pint, at a temperature of 65° ; but despite extreme care in every particular and the most judicious treatment, the attacks of fever recurred. I saw him in consultation with Drs. W. W. Johnston and Busey, of Washington, on December 23, 1889. For a few days subsequently the hepatic fever was intense, the chills occurred more than daily; the subsequent fever was very high (104° to 105°) and the sweats profuse. On Friday, the 27th, he was extremely feeble and ill, and the chilliness and sweating were almost constant. He had a strong call to stool and passed six ounces of offensive, decomposed pus. On Saturday night he passed eight ounces of the same material. Following this discharge he made a gradual but complete recovery. The diagnosis of hepatic abscess in this case was supported by the exclusion, after repeated and searching examination, of any other source for the pus.

We have thus seen illustrations of various lesions in connection with which hepatic fever may present itself. We have also seen that similar lesions may exist without the production of this particular type of pyrexia. An

attempt has been made to indicate some points of interest and importance in connection with the mechanism of its production. It has been assumed that this hepatic fever is not of very frequent occurrence, but although I may have happened to meet with a larger number of cases than should rightly fall to my lot, I am sure that it is not nearly so rare as has been represented. It seems important to place on record all carefully observed cases on account of the extreme difficulty in the differential diagnosis of the lesions, as well as in connection with the explanation of this type of fever and with the special conditions of the liver as regards its antiseptic secretion and its ptomaine-destroying function.

I will not attempt to speak fully to you of Weil's disease. This affection has only in the last few years been described as a separate entity; I do not think it comes properly at all under the class of cases I am describing. Everything connected with it seems to me to prove that it is a special infectious disease which requires much more close study in the hope of isolating the peculiar poison which produces it. The conclusions of all who have seen many cases are that it comes under the class of infectious fevers. It begins abruptly; it is attended with slight enlargement of the liver, and great enlargement of the spleen, and marked alteration of the blood. Between the fifth and seventh days the temperature falls, sometimes reaching the normal. About the tenth or twelfth day, there may be an accession of fever, though not a true relapse. There are characteristic pains in the limbs, especially in the calves, rendering motion intolerable. Jaundice is the most characteristic symptom. There is a difference of opinion as to whether the jaundice is from obstruction or alteration of the blood; my own judgment favors the latter view. There may be nephritic symptoms—albumin, tube-casts, and blood in the urine

are common and very serious symptoms. Bronchitis, epistaxis, purpura, have all been observed as accidental complications. The disease has been observed in vigorous men of middle age; rarely in women and children.

One case, clearly to me of this nature, I find I have recorded in 1883 under the title of "acute infectious jaundice"—a name which I would at present suggest for this disease, until its nature is more accurately determined.

This occurred in the case of a travelling salesman, thirty-eight years of age, of muscular frame and excellent general health, whom I saw in consultation in the north-eastern part of Philadelphia, a healthy district. He had suffered from some malarial symptoms in previous years, but not recently, and during his last journey had not been in a malarial district. He had not been especially fatigued, and no reason could be assigned for the onset of the disease, which made its appearance immediately on his return to his home.

I found the patient, on the evening of the third day, with a temperature of 105° , with a wild, excited expression, injected eyes, wildly delirious, with a strong tendency to walk up and down the room, requiring the efforts of several men to restrain him. He complained of severe pain in the head and through the frame generally. He was already intensely jaundiced, the discoloration being peculiarly deep. This continued with increasing depth until his death, on the sixth day. He had already vomited several times; the stomach was non-retentive during the second day, but subsequently, with the deepening mental dulness, the stomach became quiet. The temperature sank to 102° on the third day, and continued to fall until toward death, when there was a rise again. The tongue was heavily coated, and soon became brown and dry. There were no pulmonary symptoms. The bowels were quiet, but responded to enemata.

The spleen was distinctly swollen; the liver appeared normal in size. The pulse was rapid, 130, and this rapidity continued despite the deepening stupor and symptoms of blood-poisoning. The urine was not obtained until the end of the second day. It was then found albuminous, with epithelial and granular tubercasts. The amount secreted was small and intensely bile-stained. Death occurred in deep stupor, and was preceded by convulsive twitchings. The post-mortem examination showed no lesion of the brain; hypostatic congestion of the lungs; the spleen enlarged to double its size, very dark, and somewhat softened; the liver about normal in size, unusually dark, apparently very little, if at all, softened. Microscopic examination showed marked granular disintegration of many circumscribed areas of cells. The bile-ducts were pervious, and no obstruction was found to explain the jaundice. Of course, the mucous membrane may have been swollen during life, and the swelling have disappeared after death. There were no lesions of the intestinal glands; the kidneys were engorged with blood, and presented marked changes of infectious nephritis. The case was regarded as one of infectious disease of unknown type. Unfortunately, there were at that time no facilities for examining the blood and tissues carefully for microbes.

Clearly this acute infectious jaundice, which has close relations with *icterus gravis* of the older writers and of the present German school, has no relation whatever with the type of hepatic fever which I have described. It is connected in all probability with the entrance into the system of some specific infectious organism. I mention it to limit our field of discussion of hepatic fever more closely to the points I have proposed.

In conclusion: Although, as before stated, the term "hepatic fever" is more or less a misnomer, since there

are various affections of the liver attended with other types of fever, yet there is a degree of usage which perhaps justifies retaining this name in connection with the particular paroxysmal fever I have described. It occurs at irregular intervals and is connected with angiocholitis, with more or less extensive occlusion of the ducts. At times there is no proof of the existence of pus or of septic action, although in the great majority of cases the pyrexia is associated with a purulent lesion at some point of the biliary canals. I will detain you but a moment to ask your attention to the analogy between these febrile attacks connected with the liver and "urethral fever," as it is often styled by surgeons. In doing so I will take the opportunity of referring to the admirable account of these two types of fever by Charcot, to whose instructive paper there has been comparatively little of value added. We are all familiar with the sudden explosions of high fever, 103° to 105° F., usually preceded by a chill, which may occur in persons who have been subject to prolonged vesical or urethral irritation, and where the thickening of the mucous membrane and other coats of the urinary tract has occasioned more or less occlusion associated with the production of morbid discharges. For although urethral fever may occur without a previous morbid state of the urinary passages, it is far more apt to arise in connection with such lesions. The irritation caused by the passage of a catheter or the sudden development of complete occlusion at some point of the partially obstructed passages may, under such conditions, give rise to violent outbreaks of fever which are evidently strictly analogous with those we have studied under the name of "hepatic fever."

I must here bring these desultory remarks to a close, trusting that the imperfect record I have presented to you will be the means of eliciting, from the immense wealth of pathological material which this city contains, fuller contributions as to the frequency of hepatic fever and as

to the various lesions with which it is most often associated. With such extended studies it is not too much to hope that the special conditions or agents which in certain cases determine its occurrence may be investigated with complete success.

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